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MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
FOSTER, CHRISTINE E	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,727	GAWAD ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16-33* is/are pending in the application.

4a) Of the above claim(s) *25-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 16-24* is/are rejected.

7)☒ Claim(s) *1-13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/12/06, 9/18/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 6/12/06, is acknowledged and has been entered. Claims 1, 3-5, 21, and 23 were amended. Claims 14-15 were canceled. Claims 1-13, 16-33 are pending in the application, with claims 25-33 currently withdrawn.

Information Disclosure Statement

The Examiner thanks Applicant for providing copies of the references cited on the IDS of 9/13/02. The previous Office action incorrectly stated that copies were not originally provided, when in fact they had been received by the Office on 9/18/02. The references have been considered by the examiner as indicated on the attached form PTO-1449. It is noted that the US Patent references as well as Cite No. 22 have been lined through to avoid duplication citation since the Examiner previously indicated that the references were considered (see the Office action mailed 1/12/06).

Applicant's Supplemental Information Disclosure Statement filed 6/12/06 has been received and entered into the application. The references therein have been considered by the examiner as indicated on the attached form PTO-1449.

Objections/Rejections Withdrawn

2. The objections to claims 2-13, 16-17, 19, 21, and 23 set forth in the previous Office action are withdrawn in response to Applicant's amendments.

3. The rejections of claims 1-24 under 112, 1st paragraph (scope of enablement) are withdrawn in response to Applicant's amendments.

4. The rejections of claims 5 and 23 under 112, 2nd paragraph have been withdrawn in response to Applicant's amendments.

5. The rejection of claim 1 under 35 USC 102(b) as being anticipated by Lawrence is withdrawn in response to Applicant's amendments, in particular the amendment of claim 1 to recite that the amount of active PAI-1/multimeric vitronectin complex in the biological fluid sample is determined.

6. The rejections of claims 1-2, 4, 6-8, 10, 14, and 23-24 under 35 USC 102(b) as being anticipated by Preissner et al. and of claims 3, 5, 9, 11-13, 15-22 as being unpatentable over Preissner et al. are withdrawn in response to Applicant's arguments.

Specification

7. The disclosure is objected to because of the following informalities: the amendment replacing the paragraph at p. 11, lines 20-25 still refers to the publication as being authored "Sockman et al.", which should read "**Stockmann** et al.".

Claim Objections

8. Claims 1-13 are objected to because of the following informalities: independent claim 1 refers to an "**active** PAI-1/multimeric vitronectin complex", while the dependent claims refer to the "PAI-1/multimeric vitronectin complex". It is suggested that consistent terminology should be used throughout the claims.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-13 and 16-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Amended claim 1 recites a biological fluid that is "whole blood, **platelet releasates, platelet plasma,** plasma, serum, **and a combination of same**", which represents a departure from the specification and claims as originally filed. Applicant indicated that support may be found for the amendment at p. 6, line 32, which discloses "whole blood, plasma, or serum". However, this passage does not disclose **platelet releasates**, **platelet plasma**, or **combinations** of the recited fluids. Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to indicate where sufficient written support may be found for the limitations indicated above. See MPEP 714.02 and 2163.06

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-13 and 16-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 1 recites "determining the amount of active PAI-1...by correlating **said amount** to the amount to the amount of active PAI-1/multimeric vitronectin complex in the sample". The claim is indefinite because the claim recites both an "amount of active PAI-1/multimeric vitronectin complex" in part (ii) as well as an "amount of active PAI-1" in part (iii), such that the reference to "said amount" in part (iii) is ambiguous. Second, if "said amount" refers to the "amount of active PAI-1", this would mean that the amount of active PAI-1 is being used in order to determine itself, which is illogical. If the step of correlating is what allows the amount of active PAI-1 to be determined, it is unclear how the amount of active PAI-1 could be compared or correlated in this correlation step if it has not yet been determined. Third, it is unclear how the two amounts are correlated in order to determine the amount of active PAI-1 in the biological fluid sample. Is the amount of the active PAI-1 being equated to the amount of complex measured? Are the two inversely related? The claim is ambiguous as to how the amount of active PAI-1 is being determined based on the process steps recited in the method, which refer only to measurement of the complex.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Sieffert et al. ("Two Functionally Distinct Pools of Vitronectin (Vn) in the Blood Circulation: Identification of a Heparin-Binding Competent Population of Vn Within Platelet a-Granules" *Blood* Vol. 88 (1996), 552-560).

Sieffert et al. teach (i) providing a sample of platelet releasates (see in particular the abstract; p. 555-557, the section "Structural, immunological, and functional analysis..."; and Figure 4) and (ii) measuring the amount of PAI-1 in complex with multimeric vitronectin in the sample by a combination of gel filtration chromatography and immunoblotting. Sieffert et al. chromatographed fresh platelet releasates on an S-300 gel filtration column to separate vitronectin protein populations by size (Figure 4A). Next, PAI-1 and vitronectin were detected in the fractionated sample using antibodies to vitronectin (MoAb 1244) and to PAI-1 (rabbit antihuman PAI-1 IgG). See also the legend to Figure 4. As seen in Figure 4A, Sieffert et al. measured the amount of PAI-1/multimeric vitronectin complex as the higher molecular weight peak; free (uncomplexed PAI-1) and monomeric vitronectin (lower molecular weight peak) were eluted separately.

Although Sieffert et al. fail to specifically disclose that the PAI-1/vitronectin complex measured is a complex of **active** PAI-1 with vitronectin, the instant specification discloses at p. 2, lines 15-20 that it is **active** PAI-1 that is bound to vitronectin. Consequently, that PAI-1 in complex with vitronectin is active is inherent (see also the previous Office action at p. 9).

With respect to the preamble of claim 1, which recites "[a] method for determining active plasminogen activator inhibitor-Type 1", and also part (iii) of the claim, in which is recited the

step of "determining the amount of active PAI-1 in the biological fluid by correlating said amount to the amount of active PAI-1/multimeric vitronectin complex", it is noted that the determination of active PAI-1 has not been construed by the Examiner as a claim limitation for the following reasons. As also discussed above under 112, 2nd paragraph, the claim states that "active PAI-1" is determined, but only sets forth method steps in which the complex of PAI-1/multimeric vitronectin is determined. The claim recites correlating amounts in order to determine active PAI-1, but it is unclear which amounts are being referred to (see 112, 2nd paragraph above) or in what manner the amounts are correlated. Given that the claims do not clearly recite any process steps that relate to the determination of active PAI-1, but rather only set forth process steps relating to the measurement of active PAI-1/multimeric vitronectin complex, the teachings of Sieffert et al., in which the PAI-1/multimeric vitronectin complex is determined, meets the claim.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-11 and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamsten (*The New England Journal of Medicine* **10** (1995), 677-678) in view of Preissner et al. (*Blood* **74**:1989-1996 (1999), of record), Declerck et al. (*Journal of Biological Chemistry* **263** (1988), 15454-15461, of record), Wiman et al. ("Plasminogen activator inhibitor 1 (PAI) is bound to vitronectin in plasma" *FEBS Letters* 242 (1988), 125-128), and Harlow et al. (Antibodies: A Laboratory Manual (1988), Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pages 555-559, 561-562, 278-581, 583, 591-592, and 605, of record).

Hamsten teaches a method of measuring the activity of PAI-1 in subjects who survived a first myocardial infarction in which high PAI-1 activity independently predicted reinfarction within three years of the primary infarction (see the paragraph bridging p. 1-2). The reference teaches that there is a cause-and-effect relation between elevated plasma PAI-1 activity and myocardial infarction, establishing that at the time of the invention, measurement of PAI-1 activity was known in the art to be used for predicting myocardial reinfarction.

The teachings of Hamsten differ from the claimed invention in that Hamsten does not specifically teach measuring PAI-1 activity by measuring active PAI-1 *in complex with multimeric vitronectin.*

Preissner et al. teach a method of measuring the amount of PAI-1 in complex with vitronectin in biological fluid samples including platelet releasates, platelet lysates, and other biological fluids (see the entire document, in particular the abstract; p. 1990, left column,

"Platelet preparation and aggregation", "Preparation of platelet releasate" and "Assay Methods"; p. 1992-1993, "Complex formation between vitronectin and plasminogen activator inhibitor-1 in platelet release"; and Figure 6).

Although Preissner et al. fail to specifically disclose that the PAI-1/vitronectin complex measured is a complex of **active** PAI-1 with vitronectin, the instant specification discloses at p. 2, lines 15-20 that it is **active** PAI-1 that is bound to vitronectin. Consequently, it is inherent that PAI-1 in complex with vitronectin is active (see also the previous Office action at p. 9).

The measurement of PAI-1/vitronectin complex in Preissner et al. differs from the claimed invention in that Preissner fail to specifically teach detecting PAI-1 in complex with the **multimeric** form of vitronectin. In the reference, a sandwich ELISA assay was used to detect the PAI-1-vitronectin complex. However, because the ELISA used polyclonal anti-vitronectin antibodies, which would not distinguish between multimeric and monomeric forms of vitronectin, Preissner et al. do not specifically teach detecting PAI-1 in complex with the **multimeric** form of vitronectin.

The prior art at the time of the invention recognized, however, that vitronectin exists in multimeric as well as monomeric forms. In fact, Preissner et al. teach multimeric (dimeric) and monomeric forms of vitronectin (p. 1991, right column). Importantly, Preissner et al. also teach that the different forms of vitronectin are immunologically distinguishable, in that the monoclonal anti-vitronectin antibody VN-P1C5 bound selectively to the non-reduced, multimeric vitronectin but not to the reduced, monomeric protein (p. 1991, right column, the first paragraph). See also the data Figure 3, where the samples were analyzed by Western blot analysis under both non-reducing conditions (allowing the multimeric form to be visualized) and

under reducing conditions (where the multimeric form is reduced to monomer). Compare Figure 3B, lanes 2 and 5, under non-reduced and reduced conditions.

Wiman et al. teaches that functionally active PAI-1 in plasma is complexed with a binding protein identified as vitronectin (see the abstract and p. 125, left column). In contrast, functionally inactive or "latent" PAI-1 has a lower apparent molecular weight of 50 kDa, which corresponds with the molecular weight predicted from the primary structure of PAI-1, indicating that inactive PAI-1 exists in free or uncomplexed form. However, it is noted that Wiman et al. do not address the issue of whether vitronectin bound to PAI-1 is monomeric or multimeric. Nonetheless, the reference is pertinent to the instant claims because it establishes that it is the functionally active, rather than the latent form, of PAI-1 that exists in complex with vitronectin.

DeClerck et al. teach that PAI-1 exists in complex with vitronectin (see the entire document, in particular the abstract), in accordance with the teachings of Wiman et al. DeClerck et al. further characterized the PAI-1-vitronectin complex and demonstrated that the complex comprises the **multimeric** form of vitronectin (see the title; p. 15454, right column; p. 15459-15461, especially at p. 15459, the right column; and the paragraph bridging p. 15460-15461). As such, DeClerck et al. teach that it is specifically the multimeric form of vitronectin that binds to PAI-1.

Harlow et al. teach that immunoassay methods can be powerful, quick and easy methods for detection and quantification of antigens (p. 555). Specifically, Harlow et al. teach that two-antibody sandwich assays, which is the assay format used by Preissner et al. above, are especially useful (p. 579).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to measure the amount of active PAI-1/multimeric vitronectin complex as a marker of disease in order to predict myocardial reinfarction. Motivation to do so comes from the teachings of Hamsten that levels of active PAI-1 correlate with disease, and from the teachings of DeClerck et al. and Wiman et al, which establish that the functionally **active** population of PAI-1 that is a disease marker exists in complex with the **multimeric** form of vitronectin, while inactive PAI-1 is not found in this complex. Since the art recognized active PAI-1 as a marker of disease, and further recognized that the active population of this marker exists in complex with multimeric vitronectin, to detect this complex as a marker of disease would have been obvious. In addition, one would be motivated to measure the amount of the PAI-1/vitronectin complex by ELISA as taught by Preissner et al. in light of Harlow, which teaches the power and ease of such immunoassay methods.

One would have a reasonable expectation of success in measuring multimeric, rather than all forms of vitronectin complexed with PAI-1 because Preissner et al. teach the monoclonal anti-Vn antibody VN-P1C5, which recognizes only dimeric (multimeric) but not monomeric or reduced vitronectin (see p. 1991, right column, the first paragraph; and Figure 3 and legend, especially at Figure 3, lanes 2 and 5).

With regard to dependent claims 2, 4, and 23, Preissner et al. teach contacting the biological fluid sample with a first antibody that binds selectively to PAI-1 (PAI-1 monoclonal antibodies) and a labeled second antibody that binds selectively to vitronectin (polyclonal anti-vitronectin IgG that is labeled with biotin). Preissner et al. further teach determining the second antibody bound to the complex by incubating the labeled (biotinylated) second antibody with

peroxidase-conjugated avidin (see p. 1990, right column, the third full paragraph in particular). See also Figure 6.

With respect to claims 3, 5, 9, and 11, the ELISA assay taught in Preissner et al. differs from these dependent claims in that Preissner et al. teach a first antibody that selectively binds to PAI-1 and a labeled second antibody that selectively binds to vitronectin, which is the converse.

However, Harlow et al. teach that in methods of detecting and quantitating antigens using a two-antibody sandwich assay, the choice of which antibody to label is determined empirically, and that both combinations of solid-phase and labeled antibody should be tried to determine which is best (p. 580, item 1).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the anti-vitronectin antibody as the solid phase antibody and the anti-PAI-1 antibody as the labeled antibody in the method of Preissner et al. because Harlow et al. teach that both combinations should be tried in order to determine which is best in a two-antibody sandwich assay method, such as that of Preissner et al.

Although Preissner et al. fail to explicitly teach that the PAI-1/multimeric vitronectin/first antibody/second antibody complex was separated from the sample prior to determining the second antibody, as in claim 4, it would be immediately apparent to one skilled in the art that the 96-well microwell plate was washed following addition of the second antibody in accordance with standard ELISA assay techniques. This is evidenced by Harlow et al. at p. 579, the second paragraph.

With regard to claims 6 and 8, Preissner et al. teach that the sample is contacted simultaneously with both the first and second antibodies in that both antibodies are bound to the complex at the time of detection.

With regard to claims 7 and 24, the PAI-1 monoclonal antibodies were immobilized (coated) onto a solid support (96-multiwell plates). These plates would be considered to be an ELISA plate since they are plates upon which the ELISA assay is carried out.

With regard to claim 10, Preissner also teach a method wherein the second antibody is non-biotinylated polyclonal anti-vitronectin IgG, and wherein the 96-microwell plate is instead contacted with peroxidase-conjugated swine (antirabbit) IgG that binds to the second antibody; in this embodiment, the peroxidase-labeled third antibody is then determined (see p. 1990, right column, the third full paragraph in particular).

19. Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamsten in view of Preissner et al., Declerck et al., Wiman et al., and Harlow et al. as applied to claim 1 above, and further in view of Forrest et al. (US 4,659,678).

As discussed above, the references teach ELISA methods using antibodies that bind selectively to PAI-1 and vitronectin. The references fail to specifically teach a method wherein the first antibody *is attached to one member of a capture pair* and in which the sample-first antibody-second antibody mixture is contacted with a solid support *on which is immobilized the other member of the capture pair.*

Forrest et al. teaches methods of immobilizing antibodies to solid phase supports for use in immunoassays. In particular, Forrest et al. teach sandwich-type immunoassays using two

antibody reagents, in which one of the antibodies is labeled and in which the other is non-covalently bound to a solid phase support (column 2, line 44 to column 3, line 68). The solid phase-bound antibody may be bound by use of a specific binding protein such as avidin or biotin, which constitute a very rapid, high affinity binding system, or by use of a third antibody directed against a reagent such as FITC that is attached to the antigen antibody; the third antibody is first linked to the solid support and then used to capture the antigen antibody (column 2, lines 52-58; column 4, line 55 to column 5, line 20). Forrest et al. further teach that the antigen is contacted with both antibodies prior to the addition of the solid phase component (see in particular column 5, lines 28-34 and column 8, lines 43-55).

Therefore, it would have been obvious to label the first antibody with avidin or biotin for immobilizing to the solid support because Forrest et al. teach that such specific binding proteins constitute a very rapid, high affinity binding system for immobilizing antibodies to solid supports. It would have been further obvious to contact the sample with the first and second antibodies and then to contact the mixture with the solid support with bound avidin or biotin because Forrest et al. teach that this is preferable. One would have a reasonable expectation of success because Forrest et al. is also drawn to sandwich-type solid phase immunoassays employing two antibodies directed to distinct epitopes of an antigen.

20. Claims 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamsten in view of Preissner et al., Declerck et al., Wiman et al., and Harlow et al. as applied to claim 3 above, and further in view of Ehrlich et al. (US 5,665,548).

Hamsten in view of Preissner et al., Declerck et al., Wiman et al., and Harlow et al. are as discussed above. The references teach an assay format in which the second antibody is indirectly labeled with peroxidase (via biotin-avidin interaction), but fail to specifically teach that the second antibody is *directly* labeled.

Ehrlich et al. teach that in sandwich immunoassays, it is well known in the art that the labeled antibody may be labeled with a directly or indirectly detectable label, and that either is suitable so long as it allows for the detection of the antibody when bound to a solid support (column 27, line 39 to column 28, line 10). Ehrlich et al. teach that a preferred direct label is an enzyme, conjugated to the antibody, which produces a color reaction, such as horseradish peroxidase (column 27, lines 47-50).

Therefore, it would have been obvious to one of ordinary skill in the art to directly rather than indirectly label the second antibody with the peroxidase label because Ehrlich et al. teach that indirect and direct labels are both suitable for sandwich immunoassays, which is the assay format used by Preissner et al. and Harlow et al.

21. Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamsten in view of Preissner et al., Declerck et al., Wiman et al., and Harlow et al. as applied to claim 3 above, and further in view of Valenzuela et al. (US 6.428,792 B1).

The references are as discussed above, which teach an assay format in which the second antibody is labeled with biotin, but fail to specifically teach that the label is a fluorophore or a luminescent material.

Valenzuela et al. teach that antibody labels known in the art also include fluorophores such as rhodamine and luminescent materials such as acridinium ester compounds (column 3, line 58 to column 4, line 7).

Therefore, it would have been obvious to one of ordinary skill in the art to employ a fluorophore such as rhodamine or a luminescent material such as an acridinium ester as taught by because Valenzuela et al. teach that such compounds are commonly known antibody labels for use in immunoassays for detection of immunocomplexes.

Response to Arguments

22. Applicant's arguments, see p. 14-18, filed 6/12/06, with respect to the rejection(s) of claim(s) 1-2, 4, 6-8, 10, 14, and 23-24 under 35 USC 102(b) as being anticipated by Preissner et al., and of claims 3, 5, 9, 11-13, 15-22 as being unpatentable over Preissner et al., have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Hamsten in view of Preissner et al., Declerck et al., Wiman et al., and Harlow et al.

Conclusion

23. No claims are allowed. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cortellaro et al. ("Increased Fibrin Turnover and High PAI-1 Activity as Predictors of Ischemic Events in Atherosclerotic Patients" Atherosclerosis and Thrombosis Vol. 13(10) (1993), 1412-1417) also teach that active PAI-1 was known in the art to be a biomarker of disease.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cfoster

Christine Foster, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 9/19/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600